REMARKS

Upon entry of the above amendment, claims 1-11, 13 and 15-16 will be pending in the captioned application. The amendments to the claims do not introduce new matter within the meaning of 35 U.S.C. §132.

Accordingly, the Examiner is respectfully requested to enter the above amendment before examination. If the Examiner has any questions regarding this submission, she is invited to telephone the undersigned attorney.

Respectfully submitted, NATH & ASSOCIATES PLLC

Bv.

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Appendix A

Claim Amendments

1. (Currently amended) Compounds A compound of formula 1

in which

R1 and R2 are both hydrogen or together form an additional bond,

R3 represents a phenyl derivative of formulae (a) or (b)

wherein

R4 is 1-4C-alkoxy or 1-4C-alkoxy which is completely or predominantly substituted by fluorine,

R5 is 1-8C-alkoxy, 3-7C-cycloalkoxy, 3-7C-cycloalkylmethoxy, or 1-4C-alkoxy which is completely or predominantly substituted by fluorine,

R6 is 1-4C-alkoxy, 3-5C-cycloalkoxy, 3-5C-cycloalkylmethoxy, or 1-4C-alkoxy which is completely or predominantly substituted by fluorine,

R7 is 1-4C-alkyl and

R8 is hydrogen or 1-4C-alkyl,

or wherein

R7 and R8 together and with inclusion of the two carbon atoms, to which they are bonded, form a spiro-linked 5-, 6- or 7-membered hydrocarbon ring, optionally interrupted by an oxygen or sulphur atom,

R9 is hydroxyl, 1-4C-alkoxy, -N(R10)H, -N(H)N(R11)R12 or -N(R13)R14,

R10 is hydroxyl, 1-4C-alkoxy or 1-4C-alkoxy-2-4C-alkyl,

R11 is hydrogen, 1-4C-alkyl, 3-7C-cycloalkyl or 3-7C-cycloalkylmethyl,

R12 is hydrogen, 1-4C-alkyl, 3-7C-cycloalkyl or 3-7C-cycloalkylmethyl,

- R13 is hydrogen, 1-4C-alkyl, 3-7C-cycloalkyl or 3-7C-cycloalkylmethyl,
- R14 is hydrogen, 1-4C-alkyl, 3-7C-cycloalkyl or 3-7C-cycloalkylmethyl,
- or R13 and R14 together and with inclusion of the nitrogen atom to which they are bonded, form a 1-pyrrolidinyl-, 1-piperidinyl-, 1-hexahydroazepinyl-ring or a ring of formula (c),

wherein

A is O, S, SO, SO_2 or NR15,

R15 is hydrogen, 1-4C-alkyl, phenyl, pyridyl, $-(CH_2)_m$ -R16 or $-(CH_2)_p$ -C(O)R17,

R16 is -N(R18)R19,

R17 is -N(R20)R21,

- R18 is hydrogen, 1-4C-alkyl, 3-7C-cycloalkyl or 3-7C-cycloalkylmethyl,
- R19 is hydrogen, 1-4C-alkyl, 3-7C-cycloalkyl or 3-7C-cycloalkylmethyl,
- or R18 and R19 together and with inclusion of the nitrogen atom to which they are bonded, form a 1-pyrrolidinyl-,

- 1-piperidinyl-, 1-piperazinyl, 1-(1-4C-alkyl)-piperazin-4-yl-, 1-hexahydroazepinyl-, 4-morpholinyl-, 4-thiomorpholinyl-, thiomorpholin-1-oxide-4-yl- or thiomorpholin-1,1-dioxide-4-yl-ring,
- R20 is hydrogen, 1-4C-alkyl, 3-7C-cycloalkyl or 3-7C-cycloalkylmethyl,
- R21 is hydrogen, 1-4C-alkyl, 3-7C-cycloalkyl or 3-7C-cycloalkylmethyl,
- or R20 and R21 together and with inclusion of the nitrogen atom to which they are bonded, form a 1-pyrrolidinyl-, 1-piperidinyl-, 1-piperazinyl, 1-(1-4C-alkyl)-piperazin-4-yl-, 1-hexahydroazepinyl-, 4-morpholinyl, 4-thiomorpholinyl-, thiomorpholin-1-oxide-4-yl- or thiomorpholin-1,1-dioxide-4-yl-ring,
- n is 0, 2, 3 or 4,
- m is 2, 3 or 4,
- p is 1, 2, 3 or 4,

- 2. (Currently amended) Compounds A compound of formula 1 according to claim 1, in which
- R1 and R2 are both hydrogen or together form an additional bond,

R3 represents a phenyl derivative of formulae (a) or (b)

wherein

R4 is 1-4C-alkoxy or 1-4C-alkoxy which is completely or predominantly substituted by fluorine,

R5 is 1-8C-alkoxy, 3-7C-cycloalkoxy, 3-7C-cycloalkylmethoxy, or 1-4C-alkoxy which is completely or predominantly substituted by fluorine,

R6 is 1-4C-alkoxy, 3-5C-cycloalkoxy, 3-5C-cycloalkylmethoxy, or 1-4C-alkoxy which is completely or predominantly substituted by fluorine,

R7 is 1-4C-alkyl and

R8 is hydrogen or 1-4C-alkyl,

or wherein

R7 and R8 together and with inclusion of the two carbon atoms, to which they are bonded, form a spiro-linked 5-, 6- or 7-membered hydrocarbon ring, optionally interrupted by an oxygen or sulphur atom,

R9 is 1-4C-alkoxy, -N(R10)H, -N(H)N(R11)R12 or -N(R13)R14, R10 is hydroxyl, 1-4C-alkoxy or 1-4C-alkoxy-2-4C-alkyl,

- R11 is hydrogen, 1-4C-alkyl, 3-7C-cycloalkyl or 3-7C-cycloalkylmethyl,
- R12 is hydrogen, 1-4C-alkyl, 3-7C-cycloalkyl or 3-7C-cycloalkylmethyl,
- R13 is hydrogen, 1-4C-alkyl, 3-7C-cycloalkyl or 3-7C-cycloalkylmethyl,
- R14 is hydrogen, 1-4C-alkyl, 3-7C-cycloalkyl or 3-7C-cycloalkylmethyl,
- or R13 and R14 together and with inclusion of the nitrogen atom to which they are bonded, form a 1-pyrrolidinyl-, 1-piperidinyl-, 1-hexahydroazepinyl-ring or a ring of formula (c),

wherein

A is O, S, SO, SO_2 or NR15,

R15 is hydrogen, 1-4C-alkyl, phenyl, pyridyl, $-(CH_2)_m$ -R16 or $-(CH_2)_p$ -C(O)R17,

R16 is -N(R18)R19,

R17 is -N(R20)R21,

R18 is hydrogen, 1-4C-alkyl, 3-7C-cycloalkyl or 3-7C-cycloalkylmethyl,

- R19 is hydrogen, 1-4C-alkyl, 3-7C-cycloalkyl or 3-7C-cycloalkylmethyl,
- or R18 and R19 together and with inclusion of the nitrogen atom to which they are bonded, form a 1-pyrrolidinyl-, 1-piperidinyl-, 1-piperazinyl, 1-(1-4C-alkyl)-piperazin-4-yl-, 1-hexahydroazepinyl-, 4-morpholinyl-, 4-thiomorpholinyl-, thiomorpholin-1-oxide-4-yl- or thiomorpholin-1,1-dioxide-4-yl-ring,
- R20 is hydrogen, 1-4C-alkyl, 3-7C-cycloalkyl or 3-7C-cycloalkylmethyl,
- R21 is hydrogen, 1-4C-alkyl, 3-7C-cycloalkyl or 3-7C-cycloalkylmethyl,
- or R20 and R21 together and with inclusion of the nitrogen atom to which they are bonded, form a 1-pyrrolidinyl-, 1-piperidinyl-, 1-piperazinyl, 1-(1-4C-alkyl)-piperazin-4-yl-, 1-hexahydroazepinyl-, 4-morpholinyl, 4-thiomorpholinyl-, thiomorpholin-1-oxide-4-yl- or thiomorpholin-1,1-dioxide-4-yl-ring,
- n is 0, 2, 3 or 4,
- m is 2, 3 or 4,
- p is 1, 2, 3 or 4,

- 3. (Currently amended) Compounds A compound of formula 1 according to claim 1, in which
- R1 and R2 are both hydrogen or together form an additional bond,

R3 represents a phenyl derivative of formulae (a) or (b)

wherein

R4 is 1-4C-alkoxy or 1-4C-alkoxy which is completely or predominantly substituted by fluorine,

R5 is 1-8C-alkoxy, 3-7C-cycloalkoxy, 3-7C-cycloalkylmethoxy, or 1-4C-alkoxy which is completely or predominantly substituted by fluorine,

R6 is 1-4C-alkoxy, 3-5C-cycloalkoxy, 3-5C-cycloalkylmethoxy, or 1-4C-alkoxy which is completely or predominantly substituted by fluorine,

R7 is 1-4C-alkyl and

R8 is hydrogen or 1-4C-alkyl,

or wherein

R7 and R8 together and with inclusion of the two carbon atoms, to which they are bonded, form a spiro-linked 5-, 6- or 7-membered hydrocarbon ring, optionally interrupted by an oxygen or sulphur atom,

- R9 is 1-4C-alkoxy, -N(R10)H, -N(H)N(R11)R12 or -N(R13)R14,
- R10 is hydroxyl, 1-4C-alkoxy or 1-4C-alkoxy-2-4C-alkyl,
- R11 is hydrogen, 1-4C-alkyl, 3-7C-cycloalkyl or 3-7C-cycloalkylmethyl,
- R12 is hydrogen, 1-4C-alkyl, 3-7C-cycloalkyl or 3-7C-cycloalkylmethyl,
- R13 is hydrogen, 1-4C-alkyl, 3-7C-cycloalkyl or 3-7C-cycloalkylmethyl,
- R14 is hydrogen, 1-4C-alkyl, 3-7C-cycloalkyl or 3-7C-cycloalkylmethyl,
- or R13 and R14 together and with inclusion of the nitrogen atom to which they are bonded, form a 1-pyrrolidinyl-, 1-piperidinyl-, 1-hexahydroazepinyl-ring or a ring of formula (c),

wherein

A is O, S, SO, SO₂ or NR15,

- R15 is hydrogen, 1-4C-alkyl, phenyl, pyridyl, $-(CH_2)_m$ -R16 or $-(CH_2)_p$ -C(O)R17,
- R16 is -N(R18)R19,
- R17 is -N(R20)R21,
- R18 is hydrogen, 1-4C-alkyl, 3-7C-cycloalkyl or 3-7C-cycloalkylmethyl,
- R19 is hydrogen, 1-4C-alkyl, 3-7C-cycloalkyl or 3-7C-cycloalkylmethyl,
- or R18 and R19 together and with inclusion of the nitrogen atom to which they are bonded, form a 1-pyrrolidinyl-, 1-piperidinyl-, 1-piperazinyl, 1-(1-4C-alkyl)-piperazin-4-yl-, 1-hexahydroazepinyl-, 4-morpholinyl-, 4-thiomorpholinyl-, thiomorpholin-1-oxide-4-yl- or thiomorpholin-1,1-dioxide-4-yl-ring,
- R20 is hydrogen, 1-4C-alkyl, 3-7C-cycloalkyl or 3-7C-cycloalkylmethyl,
- R21 is hydrogen, 1-4C-alkyl, 3-7C-cycloalkyl or 3-7C-cycloalkylmethyl,
- or R20 and R21 together and with inclusion of the nitrogen atom to which they are bonded, form a 1-pyrrolidinyl-, 1-piperidinyl-, 1-piperazinyl, 1-(1-4C-alkyl)-piperazin-4-yl-, 1-hexahydroazepinyl-, 4-morpholinyl, 4-

thiomorpholinyl-, thiomorpholin-1-oxide-4-yl- or thiomorpholin-1,1-dioxide-4-yl-ring,

n is 2, 3 or 4,

m is 2, 3 or 4,

p is 1, 2, 3 or 4,

and the salts of these compounds or a salt thereof.

- 4. (Currently amended) Compounds A compound of formula 1 according to claim 1, in which
- R1 and R2 are both hydrogen or together form an additional bond,
- R3 represents a phenyl derivative of formulae (a) or (b)

wherein

R4 is 1-2C-alkoxy or 1-2C-alkoxy which is completely or predominantly substituted by fluorine,

R5 is 1-4C-alkoxy,

R6 is 1-2C-alkoxy or 1-2C-alkoxy which is completely or predominantly substituted by fluorine,

R7 is methyl and

R8 is hydrogen,

or wherein

R7 and R8 together and with inclusion of the two carbon atoms, to which they are bonded, form a spiro-linked cyclopentane, cyclohexane, tetrahydrofuran or tetrahydropyran ring,

R9 is -N(R10)H, -N(H)N(R11)R12 or -N(R13)R14,

R10 is hydroxyl or 1-4C-alkoxy,

R11 is hydrogen or 1-4C-alkyl,

R12 is hydrogen or 1-4C-alkyl,

R13 and R14 are identical and are hydrogen or 1-4C-alkyl,

or R13 and R14 together and with inclusion of the nitrogen atom to which they are bonded, form a 1-pyrrolidinyl-, 1-piperidinyl-, 1-hexahydroazepinyl-ring or a ring of formula (c),

wherein

A is 0, S or NR15,

R15 is hydrogen, 1-4C-alkyl or $-(CH_2)_p-C(0)R17$,

R17 is -N(R20)R21,

R20 is hydrogen or 1-4C-alkyl,

R21 is hydrogen or 1-4C-alkyl,

or R20 and R21 together and with inclusion of the nitrogen atom to which they are bonded, form a 1-pyrrolidinyl-, 1-piperidinyl-, 1-piperazinyl, 1-(1-4C-alkyl)-piperazin-4-yl-, 1-hexahydroazepinyl-, 4-morpholinyl or 4-thiomorpholinyl-ring,

n is 2,

p is 1,

and the salts of these compounds or a salt thereof.

- 5. (Currently amended) Compounds A compound of formula 1 according to claim 1, in which
- R1 and R2 are both hydrogen or together form an additional bond,
- R3 represents a phenyl derivative of formula (a)

wherein

R4 is methoxy or ethoxy,

R5 is methoxy or ethoxy,

R9 is -N(R13)R14,

R13 is hydrogen,

R14 is hydrogen,

or R13 and R14 together and with inclusion of the nitrogen atom to which they are bonded, form a ring of formula (c),

wherein

A is O or NR15,

R15 is methyl or $-(CH_2)_p-C(O)R17$,

R17 is 1-pyrrolidinyl,

n is 2,

p is 1,

- 6. (Currently amended) Compounds A compound of formula 1 according to claim 1, in which
- R1 and R2 are both hydrogen or together form an additional bond,
- R3 represents a phenyl derivative of formulae (a) or (b)

wherein

R4 is 1-4C-alkoxy or 1-4C-alkoxy which is completely or predominantly substituted by fluorine,

R5 is 1-8C-alkoxy, 3-7C-cycloalkoxy, 3-7C-cycloalkylmethoxy, or 1-4C-alkoxy which is completely or predominantly substituted by fluorine,

R6 is 1-4C-alkoxy, 3-5C-cycloalkoxy, 3-5C-cycloalkylmethoxy, or 1-4C-alkoxy which is completely or predominantly substituted by fluorine,

R7 is 1-4C-alkyl and

R8 is hydrogen or 1-4C-alkyl,

or wherein

R7 and R8 together and with inclusion of the two carbon atoms, to which they are bonded, form a spiro-linked 5-, 6- or 7-membered hydrocarbon ring, optionally interrupted by an oxygen or sulphur atom,

R9 is hydroxyl, 1-4C-alkoxy, -N(R10)H, -N(H)N(R11)R12 or -N(R13)R14,

- R10 is hydroxyl, 1-4C-alkoxy or 1-4C-alkoxy-2-4C-alkyl,
- R11 is hydrogen, 1-4C-alkyl, 3-7C-cycloalkyl or 3-7C-cycloalkylmethyl,
- R12 is hydrogen, 1-4C-alkyl, 3-7C-cycloalkyl or 3-7C-cycloalkylmethyl,
- R13 is hydrogen, 1-4C-alkyl, 3-7C-cycloalkyl or 3-7C-cycloalkylmethyl,
- R14 is hydrogen, 1-4C-alkyl, 3-7C-cycloalkyl or 3-7C-cycloalkylmethyl,
- or R13 and R14 together and with inclusion of the nitrogen atom to which they are bonded, form a 1-pyrrolidinyl-, 1-piperidinyl-, 1-hexahydroazepinyl-ring or a ring of formula (c),



wherein

A is O, S, SO, SO_2 or NR15,

R15 is hydrogen, 1-4C-alkyl, phenyl, pyridyl, $-(CH_2)_m$ -R16 or $-(CH_2)_p$ -C(O)R17,

R16 is -N(R18)R19,

R17 is -N(R20)R21,

R18 is hydrogen, 1-4C-alkyl, 3-7C-cycloalkyl or 3-7C-cycloalkylmethyl,

- R19 is hydrogen, 1-4C-alkyl, 3-7C-cycloalkyl or 3-7C-cycloalkylmethyl,
- or R18 and R19 together and with inclusion of the nitrogen atom to which they are bonded, form a 1-pyrrolidinyl-, 1-piperidinyl-, 1-piperazinyl, 1-(1-4C-alkyl)-piperazin-4-yl-, 1-hexahydroazepinyl-, 4-morpholinyl-, 4-thiomorpholinyl-, thiomorpholin-1-oxide-4-yl- or thiomorpholin-1,1-dioxide-4-yl-ring,
- R20 is hydrogen, 1-4C-alkyl, 3-7C-cycloalkyl or 3-7C-cycloalkylmethyl,
- R21 is hydrogen, 1-4C-alkyl, 3-7C-cycloalkyl or 3-7C-cycloalkylmethyl,
- or R20 and R21 together and with inclusion of the nitrogen atom to which they are bonded, form a 1-pyrrolidinyl-, 1-piperidinyl-, 1-piperazinyl, 1-(1-4C-alkyl)-piperazin-4-yl-, 1-hexahydroazepinyl-, 4-morpholinyl, 4-thiomorpholinyl-, thiomorpholin-1-oxide-4-yl- or thiomorpholin-1,1-dioxide-4-yl-ring,
- n is 0,
- m is 2, 3 or 4,
- p is 1, 2, 3 or 4,

7. (Currently amended) Compounds A compound of formula 1 according to claim 1, in which

R1 and R2 are both hydrogen or together form an additional bond,

R3 represents a phenyl derivative of formulae (a) or (b)

wherein

R4 is 1-2C-alkoxy or 1-2C-alkoxy which is completely or predominantly substituted by fluorine,

R5 is 1-4C-alkoxy,

R6 is 1-2C-alkoxy or 1-2C-alkoxy which is completely or predominantly substituted by fluorine,

R7 is methyl and

R8 is hydrogen,

or wherein

R7 and R8 together and with inclusion of the two carbon atoms, to which they are bonded, form a spiro-linked cyclopentane, cyclohexane, tetrahydrofuran or tetrahydropyran ring,

R9 is -N(R10)H, -N(H)N(R11)R12 or -N(R13)R14,

R10 is hydroxyl, 1-4C-alkoxy or 1-4C-alkoxy-2-4C-alkyl,

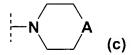
R11 is hydrogen or 1-4C-alkyl,

R12 is hydrogen or 1-4C-alkyl,

R13 is hydrogen or 1-4C-alkyl,

R14 is hydrogen or 1-4C-alkyl,

or R13 and R14 together and with inclusion of the nitrogen atom to which they are bonded, form a 1-pyrrolidinyl-, 1-piperidinyl-, 1-hexahydroazepinyl-ring or a ring of formula (c),



wherein

A is O, S or NR15,

R15 is hydrogen, 1-4C-alkyl or $-(CH_2)_p-C(0)R17$,

R17 is -N(R20)R21,

R20 is hydrogen or 1-4C-alkyl,

R21 is hydrogen or 1-4C-alkyl,

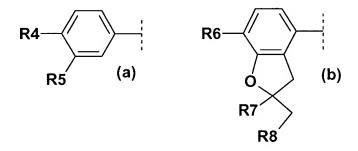
or R20 and R21 together and with inclusion of the nitrogen atom to which they are bonded, form a 1-pyrrolidinyl-, 1-piperidinyl-, 1-piperazinyl, 1-(1-4C-alkyl)-piperazin-4-yl-, 1-hexahydroazepinyl-, 4-morpholinyl or 4-thiomorpholinyl-ring,

n is 0,

p is 1,

and the salts of these compounds or a salt thereof.

- 8. (Currently amended) Compounds A compound of formula 1 according to claim 1, in which
- R1 and R2 are both hydrogen or together form an additional bond,
- R3 represents a phenyl derivative of formulae (a) or (b)



wherein

R4 is methoxy or ethoxy,

R5 is methoxy or ethoxy,

R6 is methoxy,

R7 is methyl and

R8 is hydrogen,

R9 is -N(R10)H, -N(H)N(R11)R12 or -N(R13)R14,

R10 is hydroxyl or methoxyethyl,

R11 is methyl,

R12 is methyl,

R13 is hydrogen or methyl,

R14 is hydrogen or methyl,

or R13 and R14 together and with inclusion of the nitrogen atom to which they are bonded, form a ring of formula (c),

wherein

A is O or NR15,

R15 is methyl,

n is 0,

and the salts of these compounds or a salt thereof.

- 9. (Currently amended) Compounds A compound of formula 1 according to claim 1, in which
- R1 and R2 are both hydrogen or together form an additional bond,
- R3 represents a phenyl derivative of formula (a)

wherein

R4 is methoxy or ethoxy,

R5 is methoxy or ethoxy,

R9 is -N(R10)H, -N(H)N(R11)R12 or -N(R13)R14,

R10 is hydroxyl or methoxyethyl,

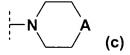
R11 is methyl,

R12 is methyl,

R13 is hydrogen or methyl,

R14 is hydrogen or methyl,

or R13 and R14 together and with inclusion of the nitrogen atom to which they are bonded, form a ring of formula (c),



wherein

A is O or NR15,

R15 is methyl,

n is 0,

- 10. (Currently amended) Compounds A compound of formula 1
 according to claim 1, in which
- R1 and R2 are both hydrogen or together form an additional bond,
- R3 represents a phenyl derivative of formulae (a) or (b)

wherein

R4 is methoxy or ethoxy,

R5 is methoxy or ethoxy,

R6 is methoxy,

R7 is methyl and

R8 is hydrogen,

R9 is -N(R13)R14,

R13 and R14 together and with inclusion of the nitrogen atom to which they are bonded, form a ring of formula (c),

wherein

A is 0,

n is 0,

- 11. (Currently amended) Compounds A compound of formula 1 according to claim 1 any of the claims 1 to 10, in which the absolute configuration (according to the rules of Cahn, Ingold and Prelog) is S in the position 4a and R in the position 8a.
- 12. (Canceled)
- 13. (Currently amended) Pharmaceutical compositions containing A pharmaceutical composition comprising one or more compounds of formula 1 according to claim 1, or a pharmaceutically acceptable salt thereof, together with a pharmaceutically acceptable auxiliary and/or carrier the usual pharmaceutical auxiliaries and/or carrier materials.
- 14. (Canceled)
- 15. (Currently amended) A method for treating an illness treatable by the administration of a PDE4 inhibitor in a patient comprising administering to said patient in need thereof a therapeutically effective amount of a compound

USSN Not yet assigned STERK Page 25 of 25

of formula 1 as claimed in claim 1, or a pharmaceutically acceptable salt thereof.

16. (Currently amended) A method for treating <u>an</u> airway <u>disorder disorders</u> in a patient comprising administering to said patient a therapeutically effective amount of a compound of formula 1 as claimed in claim 1, or a pharmaceutically acceptable salt thereof.

Appendix B

Specification Amendment

Please insert the following into the specification at page 1, line 1:

-- This application was filed under 35 U.S.C. 371 as a national stage of PCT/EP2005/050417, filed February 1, 2005. --

Appendix C

Abstract of the Disclosure

The compounds of a certain formula (1),

in which R1, R2, R3, R9 and n have the meanings as given in the description, are novel effective PDE4 inhibitors.